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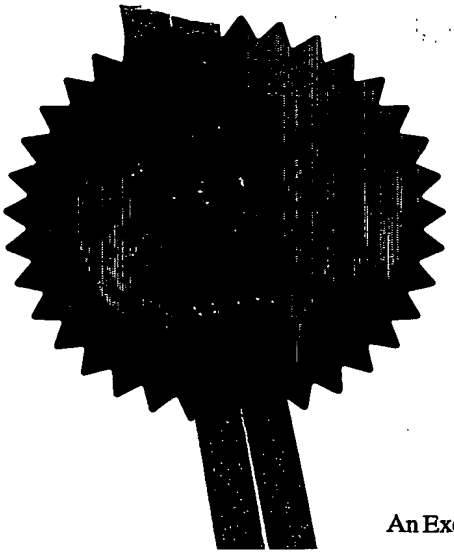

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Dated 14 April 2003

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1. Your reference — HP/CP6051932

2. Patent application number *(The Patent Office will fill in this part)* — 0209874.7

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*
Patents ADP number *(if you know it)*

UNIVERSITY COLLEGE LONDON
Gower Street
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14/5/2
pm

7986S2002

If the applicant is a corporate body, give the country/state of its incorporation — U.K

4. Title of the invention — DEVICES FOR USE IN MEDICINE

5. Name of your agent *(if you have one)* — MEWBURN ELLIS

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

YORK HOUSE
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LONDON
WC2B 6HP

Patents ADP number *(if you know it)* — 109006 ✓

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Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*
WO	PCT/GB 02/01183	26.03.02

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month /year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer "Yes" if:*
a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is not named as an applicant, or
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Claim(s)	4
Abstract	
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Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	1
for substantive examination *(Patents Form 10/77)*	
Any other documents *(Please specify)*	

11. I/We request the grant of a patent on the basis of this application.

Signature: Hughes

Date: 30 April 2002

12. Name and daytime telephone number of person to contact in the United Kingdom: HUGH C. E. PAGET — 020 7240 4405

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DUPLICAT

DEVICES FOR USE IN MEDICINE

FIELD OF THE INVENTION

This invention relates to an organ culture device for culturing a viable organ, in particular an organ consisting of or containing viable cells. The invention also relates to components which find application in the organ culture device of the invention and may find application in other uses, in particular a pump for liquid and a gas pressure control device for delivering a supply of pulsed pressurised air.

BACKGROUND OF THE INVENTION

By the term "viable organ" is here meant an organ of natural or synthetic origin which consists of or comprises living cells. The cells require culturing in order that at least they shall be maintained in a viable state and optionally grow. Such viable organs are used in medicine, in veterinary science and in other biological and biotechnical fields. The organ may be for example of natural origin, having been removed from a living creature for transplant or other purpose, or may be at least partially synthetic. For example a synthetic construct may have a synthetic substrate of biologically compatible material, on or in which cells are present. The organ may be in storage or may be undergoing culturing for the purposes of growth of the cells, for example in a synthetic construct where the cells are growing and adapting to mimic a natural organ. Our International Patent Application PCT/GB02/01183 filed 26 March 2002 describes synthetic viable organs containing cells and their manufacture.

Many methods and apparatus for maintaining cells in a viable state, for storage and/or growth, by maintaining and moving culture medium in contact with the cells are known.

SUMMARY OF THE INVENTION

The present inventors have realised that there is a need for a simple organ culture device for culturing a viable organ, in which the risk of contamination is minimised and which is easily maintained during storage and/or transport.

According to the invention in one aspect there is provided an organ culture device for culturing a viable organ, having a chamber for containing the viable organ and a conduit forming a closed liquid flow circuit with the chamber for circulation of culture medium through the chamber, the liquid flow circuit being provided with a pump for circulating the culture medium and gas-transfer means for gas transfer into and/or from the circulating culture medium.

In this device, the closed sealed liquid flow circuit provides for circulation of the culture medium over surfaces of the viable organ, while also providing for gas transfer between the exterior and the circulating culture medium, for example transfer of oxygen and if required carbon dioxide into the culture medium, or removal of carbon dioxide.

Preferably the gas transfer means operates by diffusion of gas through a gas-permeable wall of the conduit forming part of the closed liquid flow circuit. The device may therefore include a chamber, having a wall which is a gas-permeable wall of the conduit, for

containing the gas to be diffused through the gas-permeable wall.

Preferably the pump of the organ culture device is operated by pressurised gas. This is advantageous where it is desirable that the organ culture device requires no electrical power, for example during transport of the viable organ between hospitals. A simple gas-powered pump is described below.

A gas powered pump can be cheaper and is more easily disposed of than an electrically powered pump. Disposability is a significant factor, if the organ culture device must be used only once (in order to avoid risk of cross-contamination between patients).

Preferably the pump has a pump chamber for the culture medium, the chamber having a resiliently deformable wall. The pumping action is obtained by repeated deformation of the wall by pressurised gas outside the wall. The pressurised gas may be also the gas which effects gas transfer with the culture medium, and most preferably the resiliently deformable wall of the pump is itself gas-permeable, so that the gas transfer takes place through it. By combining the pumping action and the gas exchange action, a simple, economical and easily disposable device can be obtained.

In an alternative possible embodiment, the pressurised gas which operates the pump may conduct the gas exchange at a separate chamber in the culture medium circuit.

The whole of the organ culture device of the invention may be made of material which is suitable for irradiation in order to sterilise it, after its manufacture and assembly, for example using gamma-ray

radiation.

In a second aspect, the invention provides a pump for liquid, suitable for use in the organ culture device of the invention described above, but also having other possible uses. In this aspect, the invention provides a pump for liquid having a pumping chamber for the liquid and a pumping member acting on the liquid in the form of a deformable wall portion of the pumping chamber, wherein the deformable wall portion is acted on to cause pumping by pulses of pressurised gas.

Such a pump is particularly useful and effective where relatively small quantities of liquid are to be handled. Thus the pumping chamber of the pump may have a volume of not more than 1 litre, or 100 ml or less, or [illegible] ml or less. The volume of the pumping chamber is [illegible] between inlet and outlet directional flow [illegible] which are typically provided in the pump, for example one-way valves.

The pump according to the invention may comprise means for generating a pulsed pressurised gas from a source of pressurised gas such as a reservoir, e.g. a gas cylinder. A suitable device for generating such a pulsed flow of pressurised gas is described below.

The deformable wall portion of the pumping chamber is preferably a resiliently deformable tube containing the pumped liquid in use. This provides a simple construction of the device. In order to achieve gas transfer to and/or from the liquid undergoing pumping, the deformable wall portion may be gas-permeable. In this way for example, transfer of a gas such as oxygen into the liquid undergoing pumping may be achieved, where oxygenation is required. The pulsing of the pressure of

the gas acting on the deformable wall portion improves the rate of gas transfer, by generating movement of the gas.

The pump of the invention may find application in other medical or veterinary uses and apparatus, and the invention extends to such uses. The pump being simple and not requiring electrical power may be used for example to pump blood, in a cardiac assist technique, providing an extra-corporeal cardiac assist. Where oxygen transfer takes place within the pump, the pump can effect oxygenation of the blood simultaneously.

According to the invention in a third aspect there is provided a gas pressure control device for delivering pulsed pressurised gas, comprising a gas accumulator chamber having an inlet for connection to a source of pressurised gas and an outlet, the gas accumulator chamber being resiliently expansible by movement of a movable wall thereof, the device having a valve member movable between a closed position closing said outlet and an open position permitting outflow through said outlet, the device further having means actuated by the movement of the movable wall of the accumulator chamber to move the valve member from the closed position to the open position when a predetermined pressure is reached in the accumulator chamber and means for returning the valve member to the closed position upon contraction of the accumulator chamber following release of a volume of gas therefrom.

This device is self-cycling, and may require no external control, i.e. no external power source other than the supplied pressurised gas.

The resiliently expansible accumulator chamber may

be a piston and cylinder assembly, the piston providing the movable wall of the chamber. The piston may carry an actuating member which initiates movement of the valve member away from its closed position. The device may include biasing means, operating on the valve member during its movement from its closed position, whereby after removal of the pressure differential across the valve member upon its opening the valve member is moved by the biasing means to its open position. The biasing means may be an element acting in tension between the movable wall of the accumulator chamber and the valve member and arranged to bias the valve member towards its open position during the opening of the valve member.

While this gas pressure control device finds particular application in controlling t[illegible] described above, it may find other applications in medicine, and the invention extends to use of such a device in medicine and veterinary science processes and apparatus. The device may find use of example in delivering pulsed gas to a patient, for example in a positive pressure ventilation system where a patient is fed pulsed air by the mouth or nose.

The invention further provides an organ culture device as described herein in a form ready for receiving a viable organ, e.g. by manufacture of the viable organ in the culture device, the device being sterilized in readiness for housing a viable organ and contained within a sealed enclosure maintaining its sterilized state.

INTRODUCTION OF THE DRAWINGS

Embodiments of the invention will now be described by way of non-limiting example, with reference to the

accompanying drawings. In the drawings:-

Fig. 1 is a part sectional diagrammatic view of an organ culture device embodying the invention.

Fig. 2 is a sectional view of a pump, which is an embodiment of the invention and is employed in the organ culture device of Fig. 1.

Fig. 3 is a sectional view of the pump of Fig. 2, in a different phase of its operation.

Fig. 4 is a sectional view of a pressurised gas flow control device, which is an embodiment of the invention and is used in the organ culture device of Fig. 1.

DESCRIPTION OF THE EMBODIMENTS

In the drawings, the same reference numbers are used for the same corresponding parts.

The organ culture device embodying the invention shown in Fig. 1 has a viable organ in the form of a tube 1 comprising living cells embedded in a matrix of sodium alginate hardened by contact with calcium chloride solution, housed in a cylindrical chamber or cavity 8 within a housing 2. The nature of this tube 1 and the housing 2, and the method by which the tube 1 is formed *in situ* in the housing 2 is described in more detail in our International Patent Application PCT/GB02/01183 filed 26 March 2002, the contents of which are herein incorporated by reference.

The housing 2 shown in Fig. 1 has a main body part 13 which is a rectangular block having a central recess 13a whose face lies at the section line in Fig. 1, this face having a semi-circular groove 14 which forms half the cylindrical cavity 8 containing the tube 1. The

housing 2 has a second body part, not seen in Fig. 1, which fits sealingly into the recess 13a of the body part 13 and has a corresponding groove to form the other half of the cylindrical cavity 8 containing the tube 1. This cylindrical cavity extends into bores in the larger end portions 15, 16 of the main body part 13. The second body part is in place on the main body part 13 during the manufacture of the tube 1 and remains in place during the culturing of the tube 1 as described below, being intended to be removed only by the surgeon during an operation on a patient, when the surgeon wishes to use the cultured tube 1.

To manufacture the tube 1 *in situ* in the housing 2, a slider member 18 (seen in its final position in Fig. 1) is initially present at the lower end of the cavity 14 [illegible] the sleeve 21. The slider 18 has a recess in its lower end in which the narrow tube 22 at the upper end of the sleeve 21 is located.

The sleeve 21, which is sealed by O-rings (not shown) to the cavity 14 within the end portion 16 of the body 13, is carried by a block 25 so that it can be moved upwardly into the position shown in Fig. 1, from a lower position in which the slider 18 is below the level of a side passage 20.

Sodium alginate solution containing living cells (which may be cells extracted from the patient into whom later the tube 1 is to be inserted surgically) is injected through the side passage 20 (e.g. from one of the ports 23,24 described below) so as to fill the cavity 14. Then the block 25 and the sleeve 21 carrying the slider 18 is pushed upwardly to the position shown in Fig. 1. Calcium chloride solution is injected through

the conduit 28 into the interior of the sleeve 21 and emerges from the tube 22, driving the slider member 18, which acts as a regulator, upwardly along the cavity 14. The slider member 18 has an external diameter smaller than the internal diameter of the cavity 14, so that as it moves a thin layer of alginate is left behind it, which immediately contacts the calcium chloride solution and is chemically hardened sufficiently to become a shaped body (this shaped body, which is the tube 1, is not rigid). The shaped body thus consists of a matrix of hardened alginate containing the viable cells. The slider member comes to rest, as shown in Fig. 1, beyond the junction with a side passage 11. During the movement of the slider 18, excess alginate solution emerges via the cap 12.

In the block portion 25 the conduit 28 joins a side tube 26 which ends at a connector 27. Before or after the formation of the tube 1, the side passage 11 and the side tube 26 are connected by a continuous conduit 9 to form a complete closed and sealed circuit including the cylindrical cavity 14 containing the tube 1. To maintain the sealed and closed nature of this circuit, the end cap 12, the side passage 20 and the conduit 28 must be kept closed. The conduit 9 has inlet and outlet ports 23,24 with valves, which permit the simultaneous injection and removal of liquid from the closed circuit, as required in order to change or refresh the liquid of the circuit. By this means, the circuit is washed to remove the alginate solution and calcium chloride solution, and then a culture medium of a suitable nature for maintaining and promoting growth of the cells in the tube 1 is added. Suitable culture media

for this purpose are known in the art, and need not be described here.

The closed circuit formed by the cavity 14 and the conduit 9 includes a pump 3 shown in detail in Figs. 2 and 3. The pump 3 is gas-operated, using gas from a compressed gas cylinder 5 supplied via an adjustable valve 7 and a pipe 6 to a control device 4 for providing pulsed pressurised gas to the pump 3. The control device 4 is shown in detail in Fig. 4.

By means of the pump 3, which requires no mechanical or electrical power, the culture medium is circulated continuously through the closed circuit, so that the culture medium passes over at least the internal surface of the tube 1 (in practice, the tube 1 may separate from the wall of the cavity 14, so that the culture medium passes over both its surfaces). The flow of the culture medium is to some extent pulsed, since the pump 3 operates in a pulsation manner, which is believed to be advantageous for the culturing of the cells in the tube 1, if those cells in the natural state are accustomed to a pulsed flow.

The pump 3 shown in Figs. 2 and 3 has a rigid composite body 30 consisting of two end members 31, 32 of moulded synthetic plastics material, each having a connection portion 33, 34 for sealed connection to the adjacent part of the conduit 9 and each containing a one-way valve. The one way valve has a valve seat 35 and a valve member in the form of a ball 36 and biased against the valve seat by a compression spring 37. These valves therefore permit unidirectional flow through the pump 3 in the direction of the arrow 38.

Connecting the two end members 31, 32 is a rigid

cylindrical body part 39 also moulded in plastics material and having an inlet 40 and an outlet 41 for the pressurised driving gas. Within the body part 39 and sealed to the end body members 31, 32 is a cylindrical silicone rubber tube 42 having at its axial centre region a circumference recess 43 in its outer surface. The recess 43 provides a circumferential chamber extending around the tube 42 and communicating with both the inlet 40 and the outlet 41. The tube 42 at its central region thus has a thin wall portion 44 which is resiliently deformable and is much more easily deformed than the remainder of the tube 42. The outlet 41 includes a bleed orifice (not shown), to restrict the rate of flow of gas from the chamber 43.

The pump shown in [illegible] is operated solely by a pulsed supply of pressurised gas applied to the inlet 40, and produced in a manner to be described below. Each pressure pulse in the chamber 43 causes the thin wall portion 44 to be deformed resiliently inwardly as shown in Fig 3. This pushes a portion of the liquid contained in the valve chamber 45 through the one-way valve 35, 36, 37 at the right-hand side of the pump as seen in Figs. 2 and 3. As the pressure pulse declines, by leakage from the outlet 41, the thin wall portion 44 returns to its cylindrical state, drawing a volume of the liquid into the chamber 45 through the one-way valve at the left-hand end of the pump.

The volume pumped by each "stroke", i.e. each pressure pulse, can be varied by varying the dimensions of the thin wall portion 44, and also by varying the pressure variation during the pressure pulse. The pumping rate can also be varied by changing the rate of

the pressure pulses.

Any suitable gas may be used to power the pump, and no mechanical or electrical power source is required. Apart from the springs 37, the whole pump can be made of synthetic plastics material, and is therefore suitable for sterilisation e.g. by gamma-ray radiation.

In a modification of the pump, a rigid cylinder of plastics material having many apertures in its wall is inserted into the cavity 43 and presses on the end walls of the cavity 43 so that the thin wall portion 44 is maintained in a tensioned condition. This improves the resiliency of the wall portion 44 and its return to the cylindrical condition.

The silicone rubber tubing material used for the tube 42 is a conventional tubing material (AltiSil silicone tube ex. Altec, Bude, Cornwall, England) and has been found to be permeable by gases, due to gaseous diffusion. This permits diffusion of gas to or from the liquid in the pumping chamber 45. In particular, if the pumping gas used to drive the pump is or contains oxygen and/or carbon dioxide, it is possible to pass oxygen and/or carbon dioxide into the liquid in the chamber 45. In this way, when the pump is in use in the organ culture device of Fig. 1, there can be achieved in a simple and convenient manner the necessary exchange of oxygen and carbon dioxide with the culture medium circulating in the closed circuit. Alternatively, a separate gaseous diffusion device can be provided in the closed circuit, for example another portion of gas permeable silicone tube. The gas employed in the separate gas diffusion device may be the gas actually used for driving the pump of Figs. 2 and 3.

To drive the pump, it is necessary to provide a pulsed supply of pressurized gas. In the device of Fig. 1, this is achieved by a control device 4, shown in Fig. 4. Like the pump of Figs. 2 and 3, this device is powered solely by the pressured gas supplied to it and requires no other external power.

The device of Fig. 4 has a cylindrical body 50 with a peripheral gas inlet 51 and an axial outlet 52 in the end wall 53. A piston 54 is slidable axially along the cylinder 50 and sealed to the cylinder by O-rings 55. The piston 54 carries a rod 56 extending through an aperture in the second end wall 57 to stabilise the piston 54. This aperture and rod 56 are shaped to allow gas to pass in and out of the space on the left-hand side of the piston 54 as seen in Fig. 4. In this space is a compression spring 58 which biases the piston 54 towards the end wall 53.

On its front face, the piston 54 carries an axially projecting sleeve 59 having a central bore open at its front end and a closed-end slot 60 providing lateral access to the bore. Within this bore slides a rod 61 which has a pin 62 projecting into the slot 60 and carrying at its forward end a valve member 63 having an O-ring 64 and sealing against a valve seat 65 around the entrance to the outlet 52. Surrounding the rod 61 is a coil spring 66 which is connected to the valve member 63 and to the sleeve 59 and is capable of acting as a tension spring when extended and as a compression spring when in a compressed state.

The device 4 operates as follows. Gas supplied at the inlet 51 under pressure drives the piston 54 to the left, against the action of the compression spring 58, in

order to charge the cylinder chamber 67 to the right-hand side of the piston 54 with compressed gas. The valve member 63 is held against the valve seat 65 by the gas pressure differential across it. The pin 62 therefore slides along the slot 60 and the spring 66 is extended, but the tension force applied by the spring 66 is not sufficient to lift the valve member 63 from the seat 65. When the pin 62 reaches the right-hand end of the slot 60, the sleeve 59 pulls the rod 61 so that the valve member 63 is now lifted from the valve seat 65. The pressure differential across the valve member 63 thereby disappears, so that the spring 66 now pulls the valve member 63 and rod 61 rapidly to the left, opening the outlet 52 fully to allow delivery of a pulse of compressed gas from the device.

The pressure drop within the chamber [illegible] compression spring 58 to drive the piston 54 [illegible] right, carrying the valve member 63 back into contact with the seat 65, this contact being ensured by the pin 62 reaching the left-hand end of the slot 60. The spring 66 is designed so that the pin 62 is at a central region of the slot 60, in the equilibrium position.

The cycle of charging the chamber 67 and release of the gas through the outlet 52 is then repeated.

The rate of outflow of gas through the outlet 52 when open must be greater than the inflow rate through the inlet 51. This can be achieved by a suitable bleed orifice or by adjustment of the control of valve 7 shown in Fig. 1. The pressure differential across the device 4 may also control its stroke rate. The stroke rate and stroke volume can be adjusted by variation of the characteristics of the springs 58 and 66 and also the

length of the rod 61.

Apart from the spring 66, the whole device shown in Fig. 4 can be made of gamma-ray sterilisable synthetic plastics material.

Though shown as a separate unit, the device 4 of Fig. 6 maybe incorporated in the structure of the pump 3, providing a unitary pumping device. One or both of these devices can also be incorporated with the body 2, to provide a unitary construction.

As described, the components 2, 3, 4 require no external power source, other than the source of pressurised gas, and furthermore are suitable for sterilisation. The assembly of components, e.g. the body 2, conduit 9 and pump 3, and optionally also the valve 4, may be inserted into a sterilisable packaging enclosure, of the type used for many surgical devices, which is then sealed. Suitable packaging material is Rexam Medical Packaging Integra (Registered Trademark) Form medical thermal-forming film. The device inside the sealed package may then be sterilised, for example by gamma radiation, in a known manner. In this form, it is conveniently stored and transported when it is to be used to a laboratory for the initial stage of preparation of the viable organ, such as the tube 1. After formation of the tube 1, the device is ready immediately to commence the culturing stage by circulation of culture medium through the closed circuit, without requiring attachment of liquid lines and other devices. Contamination can be easily avoided throughout the duration of the culturing of the organ, which may require a period of many weeks.

The use of the pressurised gas for the powering of the device, this gas being sealed from the circulating

culture medium, is convenient, since the consumption of the gas is relatively small, and is easily provided by a canister or cylinder of appropriate compressed gas. The filling state of such a cylinder or canister is easily monitored, by means of a pressure gauge. Electrically powered devices, which do not lend themselves easily to sterilisation and are relatively expensive, are avoided. When the organ culture device is being transported, for example between hospitals, it is convenient that no electrical power source is required.

Apart from the cylinder or canister of pressurised gas, the organ culture device shown in Figs. 1 to 4 can be made almost entirely of parts which are made of synthetic plastics material, by injection moulding. The device is therefore cheap to manufacture, which is advantageous when the device is to be used only once. The device meets the regulatory standard being set at present for disposability of medical devices.

While the drawings show an organ culture device which contains a viable organ in the form of a tube which is made in situ in the device, the present invention is not restricted to this. The principle of operation of the device can be applied to the storage and transport of other viable organs, including organs of natural origin such as a kidney or blood vessel.

As discussed above, the pumps shown in Figs 2 and 3 and the control device for producing the pulsed pressured gas of Fig. 4 are capable of use in many other medical apparatuses and in devices and for purposes outside the medical field.

CLAIMS:

1. An organ culture device for culturing a viable organ, having a chamber for containing the viable organ and a conduit forming a closed liquid flow circuit with said chamber for circulation of culture medium through said chamber, said liquid flow circuit being provided with a pump for circulating the culture medium and gas-transfer means for gas transfer into or from the circulating culture medium.

2. A device according to claim 1 wherein said gas transfer means operates by diffusion of gas through a gas-permeable wall of said conduit.

3. A device according to claim 1 or 2 wherein said pump is operated by pressurised gas.

4. A device according to claim 3 wherein said pump has a pump chamber for said culture medium having a resiliently deformable wall, the pumping action being obtained by repeated deformation of said wall by pressurised gas outside said wall.

5. A device according to claim 4 wherein said pressurised gas effects gas-transfer into said culture medium.

6. A device according to claim 5 wherein said resiliently deformable wall of said pump is gas-permeable so that the gas transfer takes place through it.

7. A device according to any one of claims 1 to 6 in use containing a viable organ in said chamber and circulating culture medium in said liquid flow circuit.

8. A method of maintaining a viable organ for transport and storage, using an organ culture device according to any one of claims 1 to 6.

9. An organ culture device according to any one of claims 1 to 6 sterilized in readiness for housing a viable organ and contained within a sealed enclosure maintaining its sterilized state.

10. An organ culture device according to claim 3, 4 or 5 further including a gas pressure control device for controlling gas flow to provide pulsed flow of pressurized gas to said pump, the organ culture device being sterilized in readiness for housing a viable organ and contained within a sealed enclosure maintaining its sterilized stated.

11. A pump for liquid having a pumping chamber for the liquid and a pumping member acting on the liquid in the form of a deformable wall portion of said pumping chamber, wherein said deformable wall portion is acted on by pulses of pressurised gas to cause pumping.

12. A pump according to claim 11 having means for generating a pulsed flow of pressurised gas from a reservoir of pressurised gas.

13. A pump according to claim 11 or 12 wherein said

deformable wall portion is a resiliently deformable tube containing the pumped liquid in use.

14. A pump according to any one of claims 11 to 13 wherein said deformable wall portion is gas-permeable, for gas transfer between the pumped liquid and the pressurised gas.

15. A gas pressure control device for delivering pulsed pressurised gas, comprising a gas accumulator chamber having an inlet for connection to a source of pressurised gas and an outlet, the gas accumulator chamber being resiliently expansible by movement of a movable wall thereof, the device having a valve member movable between a closed position closing said outlet and an open position permitting outflow through said outlet, the device further having means actuated by the movement of the movable wall of the accumulator chamber to move the valve member from the closed position to the open position when a predetermined pressure is reached in the accumulator chamber and means for returning the valve member to the closed position upon contraction of the accumulator chamber following release of a volume of gas therefrom.

16. A device according to claim 15 wherein the accumulator chamber is a piston-and-cylinder assembly.

17. A device according to claim 15 or 16 wherein the movable wall carries an actuating member which initiates movement of the valve member away from its closed position.

18. A device according to any one of claims 15 to 17 having biasing means, operating on the valve member during its movement from its closed position, whereby after removal of the pressure differential across the valve member upon its opening the valve member is moved by the biasing means to its open position.

19. Use of a pump according to any one of claims 11 to 14 or a device according to any one of claims 15 to 18 in human or veterinary medicine.

20. An organ culture device according to claim 1 having, as said pump thereof, a pump according to claim 11.

21. An organ culture device according to claim 20 having a gas pressure control device according to any one of claims 15 to 18 for delivering pulsed pressurized gas to said pump.

22. A pump according to any one of claims 11 to 14 having a gas pressure control device according to any one of claims 15 to 18 for delivering pulsed pressurized gas thereto.

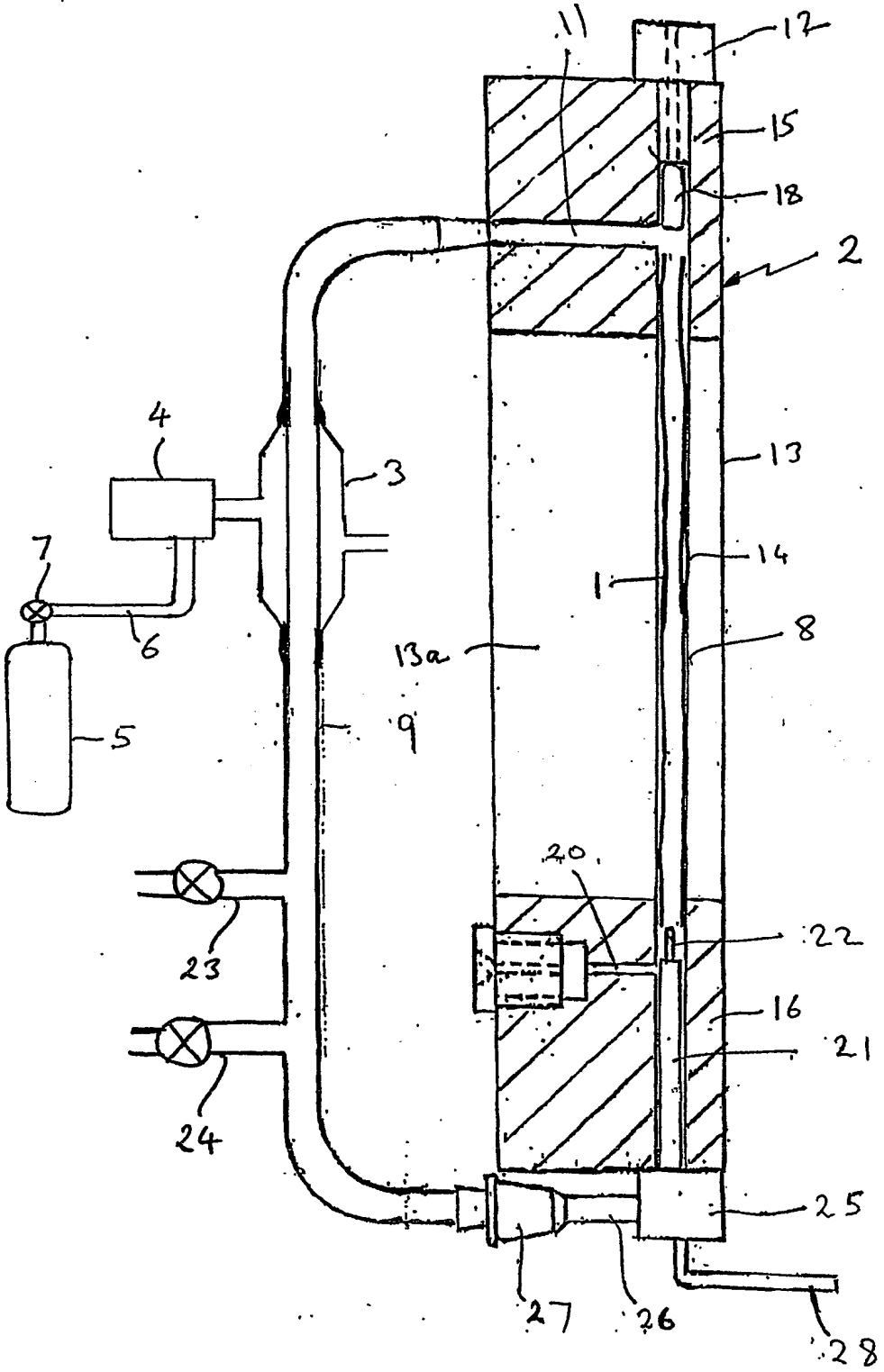

Fig. 1

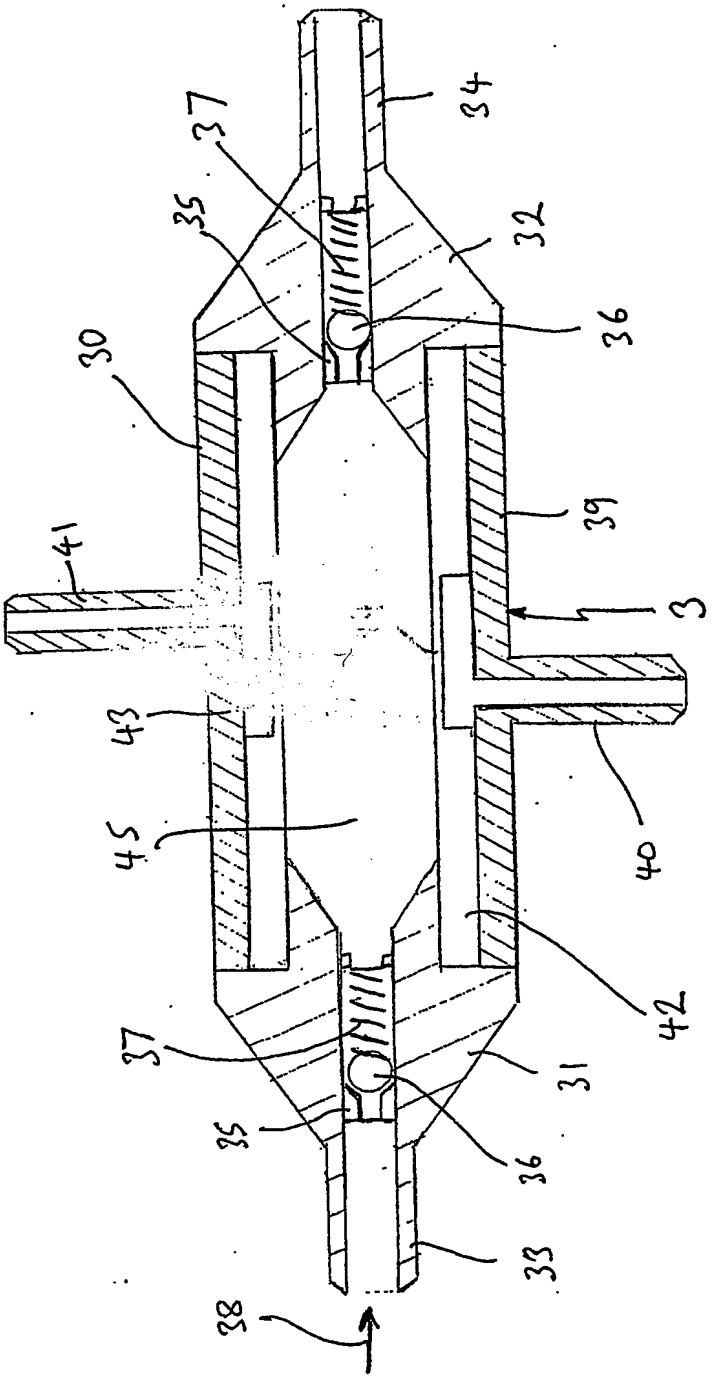

FIG. 2

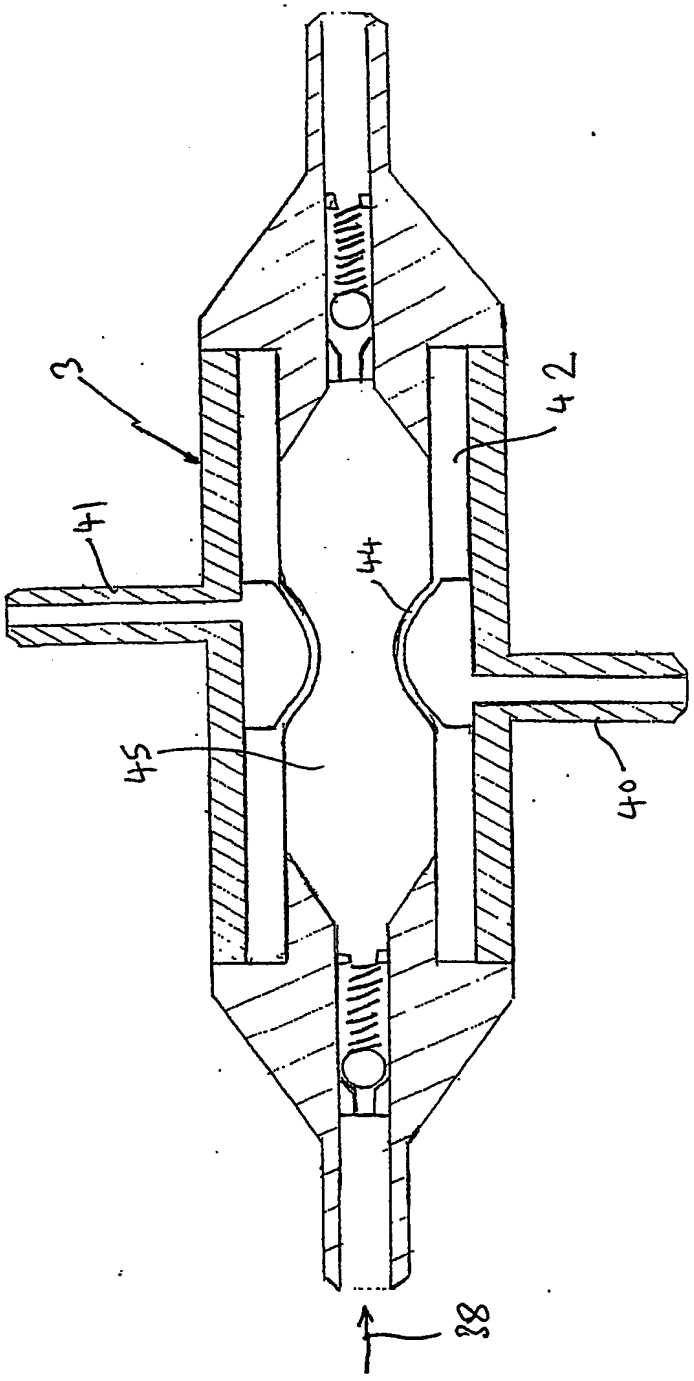

FIG. 3

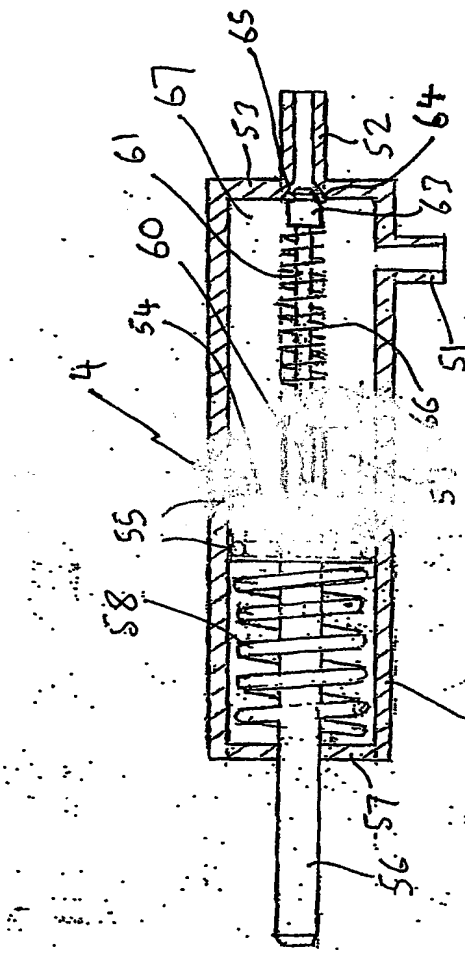

Fig. 4

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